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<b>TITLE OF CASE</b>
Polypoid cystitis in a male entire Springer Spaniel puppy
<b>SUMMARY</b>
A 14-week-old entire male Springer Spaniel was presented for haematuria. Investigations identified polypoid cystitis. Medical management failed to improve the clinical signs and the dog underwent surgical excision of the bladder polyps at 8 months old. Histopathological examination of the polyps identified granulomatous foci containing crystalline material. Eighteen months after surgery, the dog has had no further episode of haematuria and repeat ultrasound documented resolution of the lesions. This is the youngest reported case of polypoid cystitis in dogs and the first report of this lesion associated with crystal inclusions within the polyps.
<b>BACKGROUND</b>
<p>Polypoid cystitis is a relatively uncommon condition affecting adult dogs (1). This condition needs to be differentiated from neoplasias of the bladder wall, blood clots and uroliths. The animals usually present with haematuria, pollakiuria and stranguria; some dogs have no clinical signs. The polyps are commonly associated with the presence of uroliths, bacterial urinary tract infection or repeat catheterisations. It is suspected that the chronic irritation of the urothelium plays a role in the development of these lesions (1,2). In some cases, the polyps can disappear spontaneously when the concurrent disease is treated (e.g. with antibiotics, dietary change to dissolve the uroliths), supporting a causative link between the conditions (3). Other cases require surgical resection (4).</p> <p>To our knowledge, this is the first report of polypoid cystitis occurring in a young puppy. Moreover, it is the first case of polypoid cystitis in dogs where crystal inclusions have been identified on histopathology, which could provide additional information in understanding the mechanism by which these polyps develop in the bladder.</p>
<b>CASE PRESENTATION</b>
<p>A 14-week-old entire male Springer Spaniel puppy was presented to the referring veterinary surgeon with a 2-week history of progressive haematuria, mainly at the end of micturition, with no associated pollakiuria. Urinalysis from a free-catch sample collected by the referring veterinary surgeon identified an alkaline urine (pH 8), moderate haematuria and a few struvite crystals. Amoxicillin-clavulanic acid at [10mg amoxicillin/2.5mg clavulanic acid]/kg orally every 12 hours for 7 days (Clavaseptin; Vetoquinol) and glycosaminoglycan supplementation (Cystopro 1 capsule/day; Protexin) was associated with transient improvement; however, the haematuria recurred during the antibiotic treatment. A double-contrast cystogram was unremarkable. Urine bacterial culture collected at the end of the course of antimicrobials was negative. The dog was referred for further investigations.</p> <p>On admission, the dog was bright, alert and in good body condition (5.9kg, BCS 5/9). Physical examination was unremarkable. Systolic blood pressure was unremarkable (120mmHg, Doppler technique).</p>
<b>INVESTIGATIONS</b>

Serum biochemistry, haematology, coagulation tests and buccal mucosal bleeding time (BMBT) were performed to investigate a systemic cause of the haematuria. Serum biochemistry documented mild hypoalbuminemia (28.6g/L, ref. 32-38), total hypercalcaemia (3.28 mmol/L, ref. 2.30-2.60), hyperphosphataemia (3.21 mmol/L, ref. 0.75-1.25) and increased alkaline phosphatase (ALP) activity (189 IU/L, ref. <110) that were considered age-related changes. There was a mild regenerative anaemia (haematocrit 31.9%, ref. 35.0-55.0; with mild anisocytosis and polychromasia seen on the blood smear) that could be age-related or reflect recent blood loss. No haemostatic disorder was identified.

Urinalysis on a sample obtained by cystocentesis documented moderate haematuria and proteinuria (urine protein/creatinine ratio 1.12, reference range <0.5); no crystals, leucocytes or organisms were found on sediment examination. Urine bacterial culture and PCR for *Mycoplasma spp.* were negative. Abdominal ultrasound documented an irregular thickening of the cranioventral bladder wall that was polypoid in appearance (Figure 1); no uroliths were seen and the urinary tract appeared otherwise anatomically normal. Given the dog's good general condition, no further investigations were carried out and the puppy was discharged on a week course of oral meloxicam (Metacam; Boehringer Ingelheim) for suspected cystitis (0.1mg/kg SID).

One week later, the haematuria was persistent. Repeat ultrasound of the urinary tract identified progression of the lesions that were more extensive, proliferative and caused marked thickening of the bladder wall (Figure 2). Cystoscopy was carried out, identifying diffusely irregular bladder wall with a few structures that were more proliferative and polypoid in appearance. There were a few haemorrhagic lesions, some arising from the polyps and some others arising directly from the irregular bladder wall. Endoscopic biopsies were inconclusive. Incisional biopsies of the bladder wall were therefore collected during conventional cystotomy for histopathology and culture. The extent of the lesions in this small and markedly thickened bladder precluded complete excision. The nature of the lesions, neoplastic or not, needed also to be characterised prior to considering a more invasive surgery.

Histopathology documented mild, chronic interstitial cystitis with infiltration of the lamina propria by lymphocytes and plasma cells. There was a moderate to marked diffuse oedema and signs of recent haemorrhage with the presence of haemosiderophages. Bacterial and fungal cultures of bladder wall tissue were negative. Urinalysis collected by cystocentesis peri-operatively identified a moderate haematuria and the presence of struvite crystals in moderate quantity. A course of prednisolone (Prednidale; Dechra) was initiated (1mg/kg/day orally for 3 weeks, then tapered progressively over 9 weeks) as it has been reported effective in treating some dogs with proliferative urethritis whose histopathological examination had revealed similar inflammatory infiltrate (5).

The haematuria improved initially within a five days but then recurred during treatment. The puppy was re-examined at 29 weeks of age, one week after discontinuation of the corticosteroids. Physical examination, haematology and serum biochemistry were unremarkable and the dog was growing normally (12.85kg, BCS 5/9). Repeat urine bacterial culture from a sample collected by cystocentesis was negative. Repeat ultrasound of the urinary tract revealed persistence of the lesions previously identified, with a similar appearance to the previous visit (Figure 3).

## TREATMENT

In the absence of improvement with medical management, partial cystectomy was recommended to remove the polyps, for both diagnostic and therapeutic purposes. Surgery took place 3 weeks later; ultrasonographic monitoring of lesions during the period of medical management showed no overall improvement or progression of polypoid changes. The surgeon performed a ventral midline full thickness incision on the right side of the prepuce. A partial cystectomy was performed removing the pathological bladder mass (approximately 30% of the bladder wall) that appeared irregular, polypoid and haemorrhagic, whilst ensuring that the ureters were not damaged. The bladder was closed with polydioxanone suture material (PDS 3-0, Ethicon) in a simple continuous pattern. The bladder was then inflated with 20mL of sterile saline to ensure water-tight apposition.

Histopathology confirmed the lesions previously identified, with oedema and mucinous expansion of the lamina propria, some focal microhaemorrhage and scattered mononuclear inflammatory cells. In addition, there were two discrete nodular granulomatous foci, comprised of vacuolated and aggregated macrophages that were centred on an accumulation of angular, pale grey-green, birefringent, crystalline material causing refraction of the light in two slightly different directions and forming two rays (Figure 4). Bacterial and fungal cultures of the bladder wall were again negative.

Further identification of the crystals by electron dispersive spectroscopy (EDS) was attempted using scanning electron microscopy (SEM) on the histopathological slides from the bladder wall.

Although some atomic components were recognized (nitrogen, sulphur and calcium), the definitive nature of the crystals could not be determined given the thinness of the samples and the artefact background created by the glass slide. Meloxicam at 0.1mg/kg/day (Metacam, Boehringer Ingelheim) was instituted for 5 days following the surgery as an analgesic. Haematuria resolved within 10 days; pollakiuria and frequent micturition were noted post-surgery but resolved within 6 weeks.

#### **OUTCOME AND FOLLOW-UP**

Five months after the surgery, the dog was asymptomatic. Physical examination, urinalysis and urinary tract ultrasound were unremarkable. At the time of writing (eighteen months post-surgery) the dog is asymptomatic.

#### **DISCUSSION**

The signs presented in this case were consistent with polypoid cystitis, as defined in the literature as “*inflammation of the bladder mucosa and development of a polypoid mass or masses without histopathologic evidence of neoplasia*” (1). Macroscopic haematuria, as reported in this case, is the most common clinical sign (82%). Other reported clinical signs include pollakiuria, stranguria, abdominal pain or polyuria polydipsia; some dogs exhibit no clinical signs (1). Female dogs were more affected in a study including 17 dogs (88%) (1), although this sex predisposition was not confirmed in another study (6).

The mean reported age is 7 years, with the youngest canine patient reported in the published literature being 2 years old (1,6,7). The dog reported here was 14 weeks old, and is therefore, to our knowledge, the youngest case reported. On ultrasound examination a pedunculated mass or masses is most typically identified in the cranioventral bladder, though diffuse wall thickening is also occasionally noted (Martinez et al., 2003). Definitive diagnosis requires histopathology. Common histopathological findings observed with polypoid cystitis include « *polypoid projections of the mucosa and stroma into the lumen, evidence of epithelial proliferation (...), stromal edema, inflammation, stromal hemorrhage, hemosiderin accumulation, [as well as] (...) intraepithelial lumina often filled with proteinaceous secretions, ulcerations, erosions, granulation tissue, or epithelial atypia* » (1). Bladder masses in young dogs are most commonly reported to be neoplastic (8–10); however polypoid cystitis should also be included in the differential list for this condition.

The cause for the formation of the polyps remains unknown. Polyps have been associated with chronic irritation of the bladder mucosa by urinary tract infection or uroliths in both people and animals (1,6,11,12). In humans, polypoid cystitis has also been reported with chronic or recurrent urethral catheterisation, abdominal trauma, bladder vascular malformation or even without identified cause of recurrent mucosa irritation (2,11,13–15). A case of polypoid cystitis suspected to be secondary to *Candida albicans* infection has been recently reported in a newborn human (3). Although no bacterial culture was performed prior to the initial course of antibiotics, the progression of the lesions despite repeat negative urine and bladder wall cultures did not support a bacterial infection as the cause of the polyps. No trauma had been reported by the owners, and no congenital abnormality (vascular malformation, urachal remnant abnormality) was identified on ultrasound scan or exploratory laparotomy.

Uroliths can cause chronic irritation of the urothelium and it is suspected that this irritation could trigger the development of polyps (1,11). In this case, although no urolith had been noted on any

ultrasound scans, struvite crystals were seen infrequently in some of the urinalyses and crystalline material was identified on histopathology in granulomatous foci on biopsy of the bladder wall. Although this mechanism has not been reported previously as a cause of polypoid cystitis, we cannot exclude that the crystalluria caused repeat irritation to the urothelium, leading to an exuberant inflammatory reaction that trapped the crystals within the bladder wall and maintained the inflammatory process. Further studies on a larger number of cases are required to further investigate this hypothesis.

Initial medical management failed to resolve the clinical signs. Surgical excision was considered when the dog had grown sufficiently to allow complete removal of the lesions. Surgery was undertaken to prevent ongoing blood loss from the bladder wall and avoid recurrent urinary infections (1,4). Furthermore, some evidence published in the human literature suggests that chronic inflammation associated with polypoid cystitis may predispose to the development of bladder neoplasia (16). Eighteen months after surgery, the dog had had no further episode of haematuria. Recurrence of polypoid cystitis can occur in dogs, sometimes months after treatment, and regular monitoring is therefore advised (1).

#### **LEARNING POINTS/TAKE HOME MESSAGES**

- This is the first report of polypoid cystitis in a puppy. This condition must therefore be included in the differential diagnosis of haematuria and bladder masses, even in a young puppy.
- Although urinary tract infections are frequent causes of polypoid cystitis, some other conditions causing chronic irritation of the bladder mucosa also need to be investigated.
- Surgery is sometimes necessary to remove the polyps, and is usually associated with a good long-term prognosis.

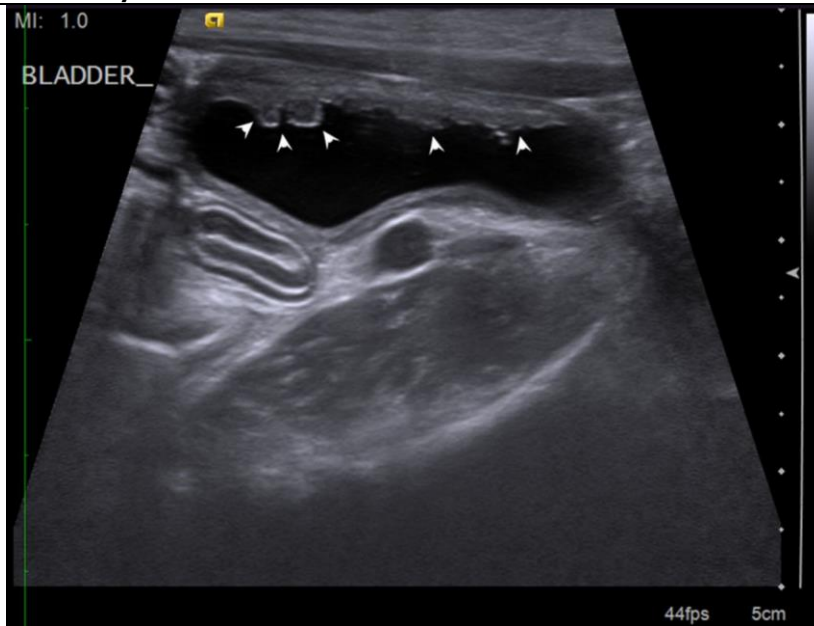
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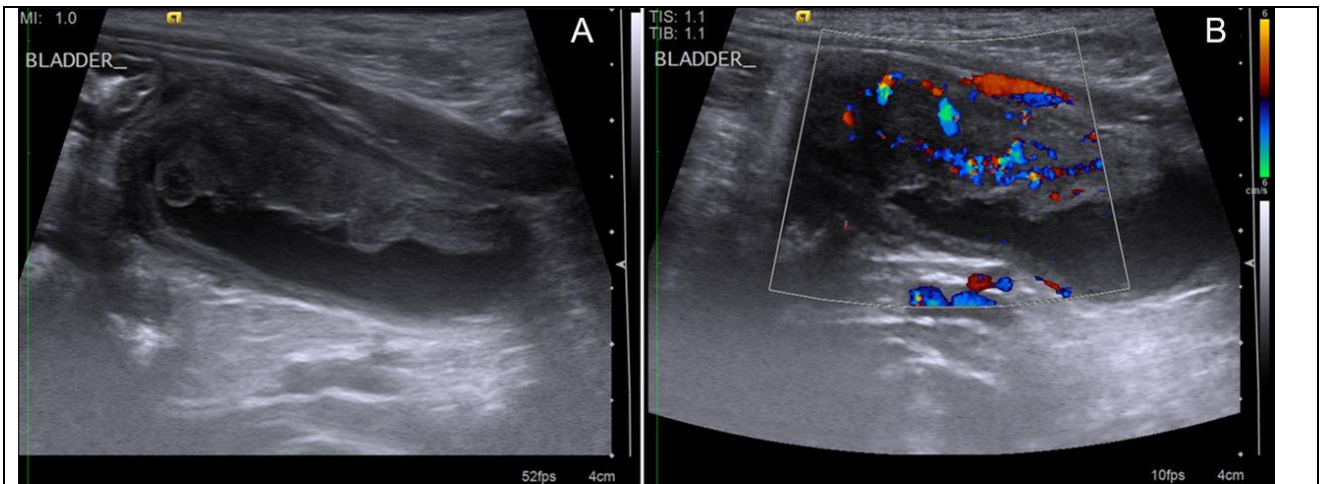
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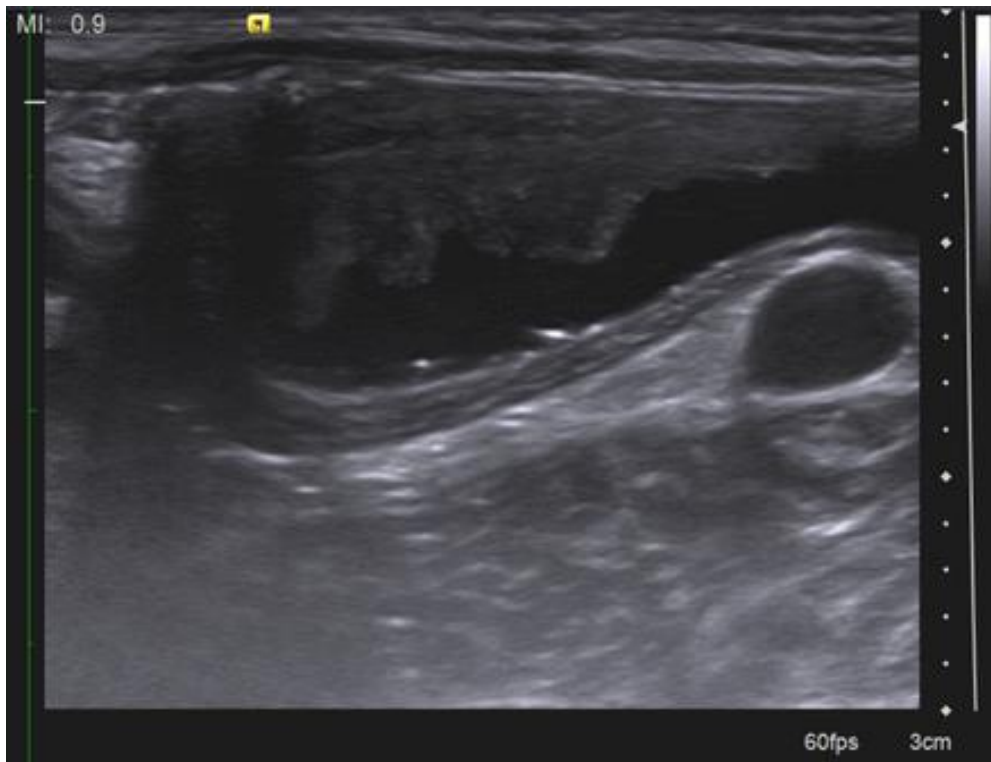
#### FIGURE/VIDEO CAPTIONS



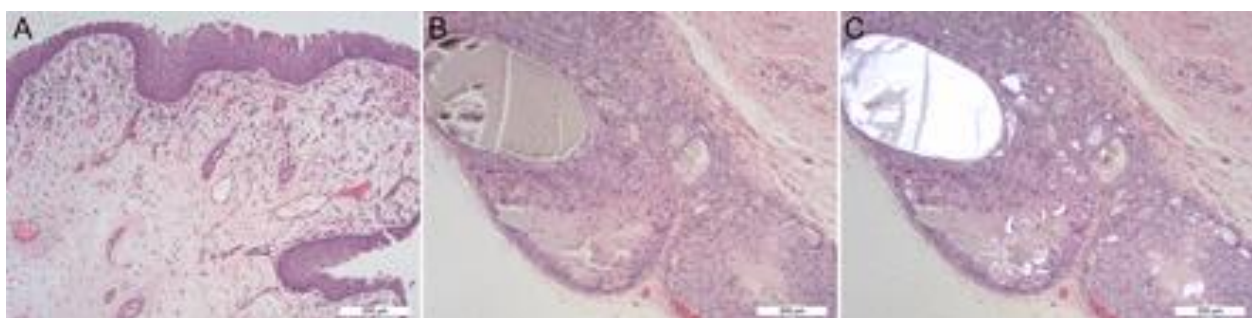
**Fig. 1.** Transverse plane ultrasound image at the level of the mid body of the bladder at the initial visit on the day of referral (15 weeks of age); the ventral wall (arrowheads) shows irregular and occasionally polypoid thickening, predominantly associated with the mucosal layer.



**Fig. 2.** Transverse plane ultrasound images at the level of the mid body of bladder at the second visit after 1 week of meloxicam (16 weeks of age); the proliferative lesions have significantly progressed compared to the Fig. 1 with more marked wall thickening (A). Doppler examination revealed the abnormal tissue to be highly vascularised (B).



**Fig. 3.** Sagittal plane ultrasound image of the bladder at the third visit at the end of the 12-week course of prednisolone (29 weeks of age); the proliferative lesions have persisted despite the medical treatment.



**Fig. 4.** Histopathological examination of the bladder wall lesions (resected surgically at 32 weeks of age). Histology, haematoxylin-eosin stain. Bar = 200 µm.

**Fig. 4A.** Proliferation of the mucosal surface with oedema and mucinous expansion of the lamina propria.

**Fig. 4B.** Nodular granulomatous focus, composed of vacuolated and aggregated macrophages that are centred on an accumulation of birefringent, angular, pale grey-green, crystalline material.

**Fig. 4C.** Same view to Fig. 4B with polarised light, showing the crystalline material in bright-silver, surrounded by granulomatous inflammation.